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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,435	03/20/2001	Kerstin Krieglstein	MBP-005XX	1324

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	7

DATE MAILED: 10/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,435	KRIEGLSTEIN, KERSTIN	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

1. Claims 1-2, 5, 7 and 11 are objected to because they recite "TGF-β" which should be changed to "transforming growth factor β". The proper name should be used in the first occurrence of a term used in the claims.

2. Claims 3 and 9 are objected to because they recite "CNS-disorder" which should be changed to "central nervous system". The proper name should be used in the first occurrence of a term used in the claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claim 1-4 and 9-10 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 5-8 and 12-13 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising a compound capable of inhibiting the biological activity of TGF-β on pre-damaged neurons, the specification does not provided enablement for a composition comprising a compound capable of inhibiting the biological activity of TGF-β on pre-damaged neurons and a second compound selected from the group consisting of urokinase and tissue plasminogen activator. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 5-8 and 12-13 are drawn to a pharmaceutical composition containing in pharmaceutically effective amounts a compound capable of inhibiting the biological activity of TGF-β on pre-damaged neurons and a second compound for disintegrating blood clots.

The specification fails to teach how to formulate the claimed pharmaceutical composition.

The specification does not disclose how to formulate the pharmaceutical composition nor does the specification teach what dosages are required to treat a patient with a peripheral or a central nervous system disorder? This demonstration is required for the skilled artisan to be able to use the claimed pharmaceutical for their intended purpose of treating peripheral or central nervous system disorders. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed pharmaceutical composition, what mode of administration can be used in regard to the pharmaceutical compositions so that the target organs necessary to treat a peripheral or a central nervous system disorder can be reached. It is unclear as to how to formulate a pharmaceutical composition which will treat any peripheral or a central nervous system disorder.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to developing a pharmaceutical composition that would achieve a desire level of success when administered to a patient

with a peripheral or a central nervous system disorder , 3) there is not seen adequate representation in the form of examples or correlations to such representations in the art which suggest the desired results of a successful pharmaceutical that is to treat any peripheral or a central nervous system disorder, 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-4 and 9-10 rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims. The claims are indefinite in the recitation of "use". It is unclear what method/process applicant is indenting to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Please note that "use of" is a Non-Statutory class of invention; However, the Examiner is viewing claims drawn to the "use of" as being drawn to products, for the purposes of art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3, 9 and 11 are rejected under 35 U.S.C. 102(b) as anticipated by Logan *(WO 93/19783, published October 14, 1993).*

Claims 1-3, 9 and 11 are drawn to a compound capable of inhibiting the biological activity of TGF-β on pre-damaged neurons, for the preparation of a medicament for treating cerebral disorders.

Logan teaches the use of anti- transforming growth factor β (TGF-β) antibodies, Arg-Gly-Asp containing peptides, decorin and its functional equivalents such as biglycan and TGF-β antagonists to prevent, treat or suppress central nervous system pathology. Logan also teaches pharmaceutical compositions containing these agents, which can be administered to patients to inhibit or enhance the production of extracellular matrix in the central nervous system (see the Abstract).

Since the Office does not have the facilities for examining and comparing applicant's compound with the compound of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the compound of the prior art does not possess the same material structural and functional characteristics of the claimed compound). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

7. Claims 1-3, 9 and 11 are rejected under 35 U.S.C. 102(b) as anticipated by Melton et al *(WO 95/10611, published April 20, 1995).*

Claims 1-3, 9 and 11 are drawn to a compound capable of inhibiting the biological activity of TGF-β on pre-damaged neurons, for the preparation of a medicament for treating cerebral disorders.

Melton et al teach the use of transforming growth factor β (TGF-β) as an antagonizing agent in a method of inducing neuronal differentiation and preventing the death and/or degeneration of neuronal cells in vitro and in vivo (page 4). Melton et al teach that the antagonizing agent of the invention can bind to growth factor and sequesters the growth factor such that it cannot bind its receptors (page 4). Melton et al teach that the invention can be used to treat neurodegenerative disorders including anoxia-ischemia (page 5).

Since the Office does not have the facilities for examining and comparing applicant's compound with the compound of the prior art, the burden is on the applicant

to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the compound of the prior art does not possess the same material structural and functional characteristics of the claimed compound). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Logan *(WO 93/19783, published October 14, 1993)* in view of *Alexander et al (Neurosurgery, 1990, 26/4, p. 559-564).*

Claims 1-13 are drawn to a pharmaceutical composition containing in pharmaceutically effective amounts a compound capable of inhibiting the biological activity of TGF-β on pre-damaged neurons and a second compound for disintegrating blood clots.

Logan teaches the use of anti- transforming growth factor β (TGF-β) antibodies, Arg-Gly-Asp containing peptides, decorin and its functional equivalents such as biglycan and TGF-β antagonists to prevent, treat or suppress central nervous system pathology. Logan also teaches pharmaceutical compositions containing these agents, which can

be administered to patients to inhibit or enhance the production of extracellular matrix in the central nervous system (see the Abstract).

Logan does not teach the use of urokinase or tissue plasminogen activator.

Alexander et al teach that urokinase and anticoagulants are recommended for treatment when patients are at risk for cerebral hemorrhage. Alexandria et al teach that tissue plasminogen activator is effective in lysing blood clots in animals.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the urokinse or tissue plasminogen activator of Alexandria et al to the pharmaceutical compositions of Logan because Alexander et al teach that urokinase and anticoagulants are recommended for treatment when patients are at risk for cerebral hemorrhage and Alexander et al has shown that tissue plasminogen activator is effective in lysing blood clots in animals. It would be expected barring evidence to the contrary that the addition of urokinase or tissue plasminogen activator would disintegrate blood clots because it is well known in the art that the prevention of blood clots would be necessary for treatment of central nervous systems disorders.

Pertinent Prior Art

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Flanders et al, Progress in Neurobiology, Vol. 54, 1998 and Krieglstein et al, Neurochemical Research, Vol. 21, 1996).*

Status of Claims

10. No claims are allowed.

Conclusion

11. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
September 29, 2002

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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